Citation:

He FJ, MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. *Cochrane Database Syst Rev.* 2004; (1): CD004937. PMID: 15266549

PubMed ID: 15266549

Study Design:

Meta-analysis or Systematic Review

Class:

M - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

This review was conducted to assess how a modest salt reduction affects blood pressure in hypertensives and normotensives and whether there is a dose-response as salt intake is reduced.

Inclusion Criteria:

- Subjects must have been randomized to have usual salt intake or a modest reduction of salt
- No concomitant interventions in either group (medications for any condition and non-pharmalogical treatments)
- Net reduction in 24-hour urinary sodium of greater than or equal to 40mmol (2.4 grams) of salt daily
- Studies with a duration of four or more weeks for salt reduction.

Exclusion Criteria:

- Studies that were excluded were those of short duration (less than four weeks)
- Children and pregnant women were excluded, as were studies that had concomitant therapies.

Description of Study Protocol:

Design

Meta-analysis

Data Extraction

- Two researchers extracted the data using a standard form. A third reviewer resolved differences
- Relevant data were study characteristics, type of study, method of blinding, length of the

study, and pre- and post-intervention results
- For pooled analyses, the researchers recorded statistics that could help estimate the variances of outcome measures.

Statistical Analysis

- Outcome measures were net changes in systolic and diastolic blood pressure and 24-hour urinary sodium excretion. These measurements were calculated as the difference between reduced salt intake and usual salt intake for mean change from baseline for parallel trials.
- In crossover trials, net changes were determined by the mean differences between the end of reduced salt and usual intake periods
- The authors also assessed plasma renin activity, aldosterone, noradrenaline and lipids
- For each trial, the variance of the treatment effect for blood pressure was calculated. This measurement was obtained from standard deviations or standard errors of paired differences between baseline and end of follow-up for parallel trials or between two treatment periods in a crossover trial. If such data were not provided, confidence intervals and exact T or P-values were used.
- For studies where the exact variance of paired difference was not derivable, the value was imputed by inverting a boundary P-value ($P<0.05$ became $P=0.05$) or by assuming a correlation coefficient of 0.5 between the initial and final blood pressure. 10 of the 31 trials in this meta-analysis required imputed variance.
- Mean effects were calculated with fixed and random effects models on Cochrane Collaboration Review Manager software
- To assess for dose-response relationships between change in 24-hour urinary sodium and change in blood pressure, weighted linear regression was used, assuming a zero intercept. When the authors performed weighted linear regression without fixing the origin, the intercepts were not significantly different from zero.
- Plot asymmetry was used to find publication or other biases.

Data Collection Summary:

Search method

The authors had a search strategy that they developed in a prior year. They searched MEDLINE, EMBASE, CINAHL, and the Cochrane Library. 33 specific search terms were used to find original research articles and there were no language restrictions.

Description of Actual Data Sample:

Initial N

- 20 trials with hypertensive individuals (N=802)
- 11 trials with normotensive individuals (N=2,220)

Attrition (final N)

31 trials (N=3,022)

Age

Median age 50 years for all trials (range of 22 to 73 years)

Ethnicity

Other relevant demographics

Anthropometrics

Location

Not applicable since this is a meta-analysis

Summary of Results:

1. Effect on blood pressure

Trials in individuals with elevated blood pressure: 20 trials included 802 subjects. Crossover design was used in 14 studies and parallel design in the other six. Median age was 50 years (24 to 73 years for a range). 12 studies were double-blind, seven were blood pressure observer blind, and one did not report blinding. Median blood pressure on usual salt intake was 149/94mm Hg. Study duration was one month to one year. Median 24-hour urinary sodium on usual salt intake was 162mmol of salt daily (9.5 grams), with a range of 125 to 191mmol per day (7.4 to 11.2 grams). On the reduced salt diet, the median 24-hour urinary sodium was 87mmol per day of salt (5.1 grams), ranging from 57 to 125mmol per day (3.4 to 7.4 grams).

Median net change in 24-hour urinary sodium was -78mmol of salt daily (4.6 grams), ranging from 53 to -117mmol of salt daily (3.1 to 6.9 grams). The average reduction in salt intake was similar to public health recommendations.

The pooled estimates of changes in blood pressure were -5.06mm Hg (95% CI: -5.81 to -4.31) for systolic and -2.70mm Hg (95% CI: -3.16 to -2.24) for diastolic. Pooled estimates of blood pressure changes using the random effects model was -5.27mm Hg (95% CI: -6.69 to -3.85) for systolic and -2.76mm Hg (95% CI: -3.55 to -1.97) for diastolic.

Significant changes were noted from dose-response analysis with salt reduction and systolic and diastolic blood pressure. A reduction of 100mmol per day in salt intake (6 grams) predicts a decrease in blood pressure of 7.2mm Hg (95% CI: 5.6 to 8.8) for systolic and 3.8mm Hg (95% CI: 2.8 to 4.7) for diastolic blood pressure.

Trials in individuals with normal blood pressure: 11 trials included 2,220 subjects, in which the median age was 47 years (22 to 67 years). Six of these trials used crossover design, and the other five used parallel comparisons. Seven trials were double-blind and four were blood pressure observer blind. The studies were from one month to three years. Median blood pressure on usual salt diet was 127/78mm Hg. Mean 24-hour urinary sodium was 154mmol per day of salt (9.1 grams), with a range of 128 to 200mmol per day (7.5 to 11.8 grams). The mean 24-hour urinary sodium on the reduced salt diet phase was 82 mmol per day (4.8 grams), ranging from 56 to 135mmol per day (3.3 to 7.9 grams). A reduction in salt of 100mmol per day (6 grams) predicts a fall in blood pressure of 3.6mm Hg for systolic and 1.7mm Hg for diastolic.

Trials in all individuals: A fixed effects model found the following changes in blood pressure: -3.03mm Hg (95% CI: -3.46 to -2.59) for systolic and -1.76mm Hg (95% CI: -2.07 to -1.46) for

diastolic. The random effects model found a change of -3.99mm Hg (95% CI: -5.05 to -2.93) for systolic and -1.92mm Hg (95% CI: -2.59 to -1.26) for diastolic.

2. Effect on hormones and lipids
Plasma renin activity: 11 trials reported plasma renin activity (eight studies on hypertensives and three on normotensives). Median plasma renin activity was 0.97ng/ml per hour on the usual salt intake and 1.53ng/ml per hour on reduced salt diet. The fixed effect model found a pooled estimate of change of 0.13ng/ml per hour (95% CI: 0.009 to 0.18). The random effects model found 0.29ng/ml per hour (0.15 to 0.42).

Aldosterone: Nine trials studied plasma aldosterone (seven studies with hypertensive subjects and two with normotensives). Median plasma aldosterone was 298pmol/l on usual salt intake and 399pmol/l on reduced salt intake. Pooled estimate of change in aldosterone was 90.7pmol/l (95% CI: 68.1 to 113.3) with the fixed effect model and 122.3pmol/l (95% CI: 60.7 to 183.8) with the random effects model.

Noradrenaline: This value was measured in six trials. One trial showed a significant increase of 79 pg/ml ($P<0.05$), and the other trials observed no significant changes.

Lipids: Five trials reported total cholesterol and three reported triglycerides, LDL and HDL. There were no significant changes noted in any lipid values.

3. Study quality
23 trials of 31 had adequate concealment of treatment allocation. Eight trials did not report this information. Only seven trials used intent-to-treat analysis. Of all the trials, 19 were double-blind and 11 were blood pressure observer-blind. One small trial in hypertensives was non-blind. When the latter study was excluded and the data re-analyzed, the results were unchanged. The mean net change in blood pressure for hypertensive subjects was -5.04mm Hg (95% CI: -5.79 to -4.28) for systolic and -2.72mm Hg (95% CI: -3.18 to -2.27) for diastolic after the non-blinded study was excluded.

4. Publication bias
The authors used funnel plots to plot the treatment effect against the reciprocal of the standard error of the treatment effect. The funnel plots were symmetrical for diastolic blood pressure for the mean effect size line (asymmetry test: P=0.500). The systolic plot was suggestive of bias (asymmetry test: P=0.034). The authors determined that the smaller effects were likely due to smaller reduction of salt intake achieved in longer-term trials. When the two trials were removed from the analysis, the asymmetry test was not significant.

5. Dose response to salt reduction
Weighted linear regression with the regression line forced through the origin showed a significant dose response between reduced salt intake and the fall in blood pressure, which may mean that there is a greater effect on blood pressure as salt intake continues to be lowered.

The authors emphasize that the best way to assess dose response between salt intake and blood pressure is to review blood pressure responses to several levels of salt intake for a long period of time. Few controlled trials have used this method. The findings from these authors support the findings from these few other studies, which is that blood pressure is lowered with reduced salt intake.

6. Adverse side effects of modest salt reduction
This meta-analysis found no adverse side effects.

7. Evidence supporting reduction in population salt intake
The authors support reduction of dietary salt intake for all individuals and suggest a gradual reduction of salt content in processed foods. This salt reduction would require no change on the consumer's part, and it would not be detectable.

Author Conclusion:

Even a modest reduction in salt intake significantly lowers blood pressure in hypertensive and normotensive individuals. This review found a dose-response to reduced salt intake. Salt intake is recommended by these authors to be 3 grams daily for the strongest effects.

Reviewer Comments:

Blood pressure continues to decrease as salt intake decreases. These results could be applied population-wide, not only for individuals with high blood pressure.

Research Design and Implementation Criteria Checklist: Review Articles

Relevance Questions		
1.	Will the answer if true, have a direct bearing on the health of patients?	Yes
2.	Is the outcome or topic something that patients/clients/population groups would care about?	Yes
3.	Is the problem addressed in the review one that is relevant to nutrition or dietetics practice?	Yes
4.	Will the information, if true, require a change in practice?	Yes

Validity Questions		
1.	Was the question for the review clearly focused and appropriate?	Yes
2.	Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search termsused described?	Yes
3.	Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased?	Yes
4.	Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible?	Yes
5.	Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined?	Yes
6.	Was the outcome of interest clearly indicated? Were other potential harms and benefits considered?	Yes

7.	Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issued considered? If data from studies were aggregated for meta-analysis, was the procedure described?	Yes
8.	Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included?	Yes
9.	Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed?	Yes
10.	Was bias due to the review's funding or sponsorship unlikely?	Yes